Case Report

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Oriental Cholangiohepatitis in a Caucasian male

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Abstract

Recurrent pyogenic cholangitis (RPC) is a condition found almost exclusively in individuals who lived in Southeast Asia. We report a case of a Caucasian veteran diagnosed with RPC after presenting with a 5-year history of recurrent fevers and abdominal pain 20 years after serving in Japan, South Korea, and Guam. Extensive evaluation led to the diagnosis of RPC with improvement after biliary decompression and antibiotics. Although rare, RPC should be considered in individuals who present with recurrent bouts of abdominal pain and fevers regardless of race.

Keywords

Oriental Cholangiohepatitis, recurrent pyogenic cholangitis

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Introduction

Recurrent pyogenic cholangitis (RPC), first coined in 1930, was previously known as "Oriental Cholangiohepatitis" and "Hongkong Disease" as it was found almost exclusively in people who live in Southeast Asia.[1] In the United States, documented cases are increasing in cities with immigrants coming from endemic countries.[2] However, there are no known reports of RPC in individuals who only briefly visited endemic areas. We report a rare case of a Caucasian veteran who was diagnosed with RPC 20 years after serving in Japan, South Korea, and Guam, and review the related literature on this topic.

Case report

A 47-year-old otherwise healthy Caucasian man presented with 2 days of fever, right upper quadrant pain, jaundice, acholic stools, and dark urine. He was diagnosed with cholestatic hepatitis of unknown etiology 5 years ago after being hospitalized numerous times for recurrent self-limited nausea, vomiting, fever, jaundice, and abdominal pain for which extensive investigations demonstrated only mild cholestasis, unexplained eosinophilia with a peak of 8.9%, and nonconclusive ultrasound, hepatobiliary iminodiacetic acid (HIDA) scan, computerized tomography scan, and magnetic resonance cholangiopancreatography (MRCP). Twenty years prior, he served for a total of 1 year as a post-Vietnam war marine which included travels to Japan, South Korea, and Guam. He did not recall any illnesses during his service.

Upon admission, physical exam was otherwise unremarkable except for fever of 100.3 ºF, jaundice, and right upper quadrant tenderness. Laboratory studies were notable for negative autoimmune work-up (antinuclear antibody test, antimitochondrial test), and white blood cell (WBC) count of 6.3×10^9/L with eosinophilia of 12%. Liver tests were consistent with obstructive pathology with an alkaline phosphatase of 297 U/L, total bilirubin of 13.3 mg/dL, direct bilirubin of 9.8, aspartate aminotransferase of 178 U/L, alanine aminotransferase of 407 U/L, and gamma-glutamyl transferase of 1,109 U/L. MRCP revealed left and right hepatic duct dilation and a filling defect in the proximal common bile duct suggestive of a calculus (Figure 1). Subsequent endoscopic retrograde cholangiopancreatography (ERCP) was consistent with extensive periductal fibrosis (Figure 2). Due to severe narrowing and inability to

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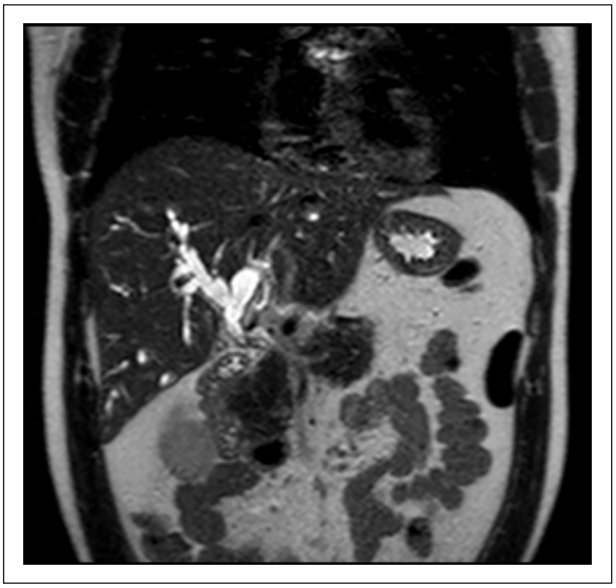

Figure 1. Magnetic resonance cholangiopancreatography without contrast of the bile ducts: The liver demonstrates intrahepatic duct dilation. The left hepatic duct measures 13 mm and the right hepatic duct measures 12 mm. There is a filling defect in the proximal common bile duct suggestive of a calculus. Contour of the bile ducts is irregular and ragged.

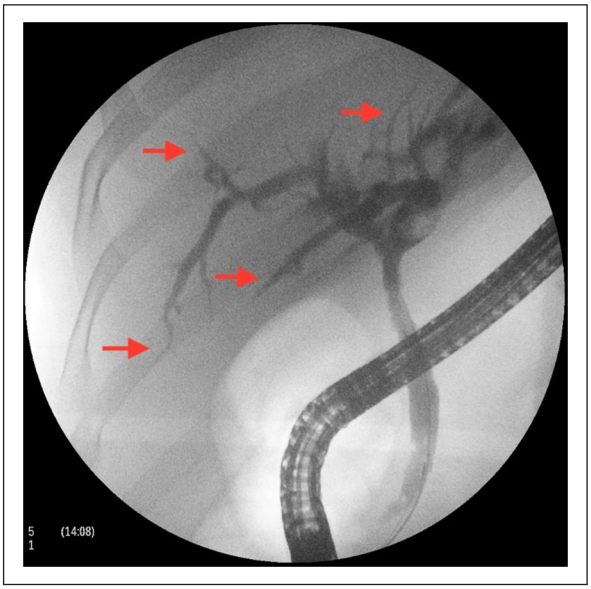

Figure 2. Endoscopic retrograde cholangiopancreatography showing the "Arrowhead sign" (red arrows). The arrowhead appearance of the bile ducts is reflected by the decreased arborization of the peripheral ducts and multiple intrahepatic biliary structures. The rapid tapering of the intrahepatic ducts resulting to less acute branching patterns is due to extensive periductal fibrosis.

access the stones via ERCP, spyglass cholangioscopy was done for further characterization of the filling defect within the intrahepatic ductal strictures which revealed a calculus encasing the entire lumen of the proximal common bile duct. Shockwave lithotripsy, sphincterotomy, and stent placement was subsequently performed for biliary decompression, and he was started on antibiotics which resolved his symptoms. Brushings from the narrow segments revealed focal reactive changes and fibrinous exudates. Bile culture was positive for *Klebsiella pneumoniae*, and cytopathology was negative for malignant cells. Two months later, he had recurrence of symptoms and was diagnosed with left hepatic lobe abscess and *E. coli* sepsis managed by percutaneous drainage and IV antibiotics. Ursodeoxycholic acid prophylaxis was started.

Over the following 3 years, he had gastroenterology follow-up every 3–6 months with subsequent repeat liver chemistries and computed tomography (CT) scans for symptom recurrence, and consequent ERCPs which revealed stent occlusion with choledocholithiasis which resolved after stent changes and shockwave lithotripsy. On the latest follow-up, he remained asymptomatic for the past 6 months.

Discussion

RPC is a recurrent syndrome of bacterial cholangitis due to biliary strictures and stone formation occurring within the intrahepatic ducts. The gallbladder is usually disease free. It commonly presents with the Charcot triad (right upper quadrant pain, fever, and jaundice) during the bouts.[1]It is strongly associated with malnutrition, low protein intake, and biliary infestation by trematodes such as *Ascaris lumbricoides* or nematodes such as *Clonorchis sinensis. C. sinensis* is a liver fluke with a lifespan of 20 years and can thus manifest itself years after initial infestation. It is endemic in China, Japan, Taiwan, Vietnam, and Korea.[1,3–5] It is postulated to cause a disruption in the bile duct's epithelial barrier leading to a cascade of transient portal bacteremia with gut flora (e.g. *E. coli, Klebsiella, Pseudomonas*, and *Proteus*), secondary stone formation, and increased biliary pressure.[6] Some studies have shown that debris of ova and parasites in the ductal system may serve as a nidus for calcium bilirubinate stone formation. Involvement usually includes the left and right hepatic lobes and the common bile duct. The left hepatic duct is more severely and frequently affected presumably due to its more horizontal configuration which may affect bile drainage.[7] The dilated intrahepatic bile ducts will feature chronic inflammation, mural fibrosis, and proliferation of peribiliary glands without extrahepatic biliary obstruction.[8,9] Repeated attacks can lead to progressive damage to the bile ducts and liver parenchyma resulting in liver atrophy, abscesses, cirrhosis, and cholangiocarcinoma.[1,6]

Clinical correlation is vital since laboratory findings may be nonspecific and can be strikingly like the more common causes of cholangitis such as primary sclerosing cholangitis. This patient's antinuclear antibody (ANA) was negative which makes an autoimmune cause unlikely. Leukocytosis and cholestatic liver abnormalities may be present.[5] Diagnosis of *Clonorchis sinensis* and *Ascaris* infection is based on

microscopic identification of eggs in stool specimens. More than one stool sample may be needed. The patient did not undergo stool testing on initial presentation which may have contributed to the delay in diagnosis. Stool tests for ova and parasites are recommended for newly diagnosed RPC, although low in sensitivity. Bile cultures almost always yield enteric bacteria.[9]

Ultrasound is the preferred initial test to demonstrate segmental biliary dilation, hepatolithiasis, and liver abscess, however, it is limited by a poor negative predictive value for RPC.[10] ERCP is both diagnostic and therapeutic and allows for the delineation of the biliary tree and definitive decompressive procedures. MRCP can be done where ERCP is difficult or impossible and is particularly useful in the evaluation of proximal ductal obstruction in cases with severe biliary stenosis. The decreased arborization of peripheral ducts, multiple intrahepatic biliary strictures, and rapidly tapering intrahepatic ducts (arrowhead sign) are better depicted on MRCP.[11] Other diagnostic clues pointing to RPC include thickening and hyperenhancement of bile duct walls, stones within both intrahepatic and extrahepatic ducts, and lobar and segmental liver parenchymal atrophy in sites of greatest biliary.[12]

Liver fluke infections carry a higher risk of cholangiocarcinoma. However, like primary sclerosing cholangitis, diagnosis of malignancy in patients with RPC can be difficult based on brush cytology alone due to the paucity of malignant cells on superficial mucosal biopsies as the result of the fibrotic reaction to the tumor and expansion into the subepithelial layers. In a study by Awadallah et.al, compared with cholangiography, cholangioscopy had significantly better sensitivity (92% versus 66%), specificity (93% versus 51%), and negative predictive value (97% versus 84%) in the diagnosis of cholangiocarcinoma, thus when used by endoscopists experienced in recognizing intraductal pathology, it can increase the diagnostic yield of tissue sampling.[13]

Spyglass cholangioscopy was utilized in this patient and allowed identification of stones within the indeterminate biliary strictures as well as assisted in targeted biopsies of bile duct lesions and clearance of intrahepatic stones.

Definitive treatment includes biliary decompression and antibiotics. While treatment with praziquantel is successful in eradicating the offending organism in 90% of the cases, this does not result in resolution of biliary fibrosis. Sphincterotomy, stricture dilation, stone removal and stent placement alleviate stasis and luminal compromise in the biliary tree. Restenosis of strictures is common when biliary stent placement is attempted due to the ongoing fibrotic changes in the thick and fibrous ductal tissues.[7] The role of the addition of Ursodeoxycholic acid in reducing calcium bilirubinate stone formation is unclear; however, it may be helpful in reducing bile viscosity and increasing bile flow.[14] RPC is a chronic disease with multiple exacerbations requiring repeated biliary dilatation and stone removal. Even after adequate biliary drainage, most patients will have progression of intrahepatic disease. Further attacks can be prevented by ERCP with or without choledocoscopy for stone retrieval.[7] Hepatic resection should be reserved for patients with anatomically limited obstructions, significant localized hepatic atrophy and fibrosis, multiple liver abscesses, or concurrent intrahepatic cholangiocarcinoma.[15] The role of liver transplant has not been extensively explored and may be an option for patients with diffuse disease.

Conclusion

This case illustrates that RPC is not limited to individuals of Asian descent. This rare form of cholangitis can mimic the initial presentation of the more common acute ascending cholangitis thus a careful history and attention to risk factors are critical to distinguish between the two. It can be suspected with a high degree of confidence based on travel history, recurrent bouts of cholangitis, eosinophilia, and bile culture yielding enteric bacteria. RPC is unique in its pathophysiology due to its de novo intrahepatic stone formation with sparing of the gallbladder. Management of this disease is a multidisciplinary challenge especially when there is a delay in diagnosis due to the extent and inaccessibility of strictures. Once prompt treatment and follow-up are initiated, patients can have more disease-free intervals with reduced burden of unnecessary hospitalizations.

Article guarantor

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Author note

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Author roles

L.S.K.S. and L.N.S. conceptualized, gathered data, performed literature review, and drafted the report. C.E.S interpreted the images and provided his clinical expertise. K.D. critically reviewed the paper. All authors reviewed the final manuscript.

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